

Rejection Under 35 U.S.C. § 112, first paragraph

Original claims 1-8 and 10-15 (new claims 16-29) have been rejected under 35 U.S.C. § 112, first paragraph, as being nonenabled with respect to the term “prodrug.” Specifically, the Office Action asserts that the choice of a “prodrug” will vary from drug to drug causing more than minimal routine experimentation to determine which prodrug will be suitable for the instant invention. It is submitted respectfully that one of ordinary skill in the art would readily be able to make and/or use a prodrug within the scope of the present invention given the Applicants’ disclosure.

For example, the Specification includes the following:

The term prodrug as used throughout this text means the pharmacologically acceptable derivatives, *e.g.* esters and amides, such that the resulting biotransformation product of the derivative is the active drug as defined in the compounds of formula (I). The reference by Goodman and Gilman (The Pharmacological Basis of Therapeutics, 8th ed., McGraw-Hill, Int. Ed. 1992, “Biotransformation of Drugs”, p. 13-15) describing prodrugs generally, is hereby incorporated.

(*see*, Specification at 3, lines 15-20). Given this guidance, there is no evidence that one of ordinary skill in the art would require anything more than routine experimentation to make a suitable prodrug falling within the scope of the claimed invention.

Based on the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. §112, first paragraph.

Rejections Under 35 U.S.C. § 112, second paragraph

Original claims 1-8 and 10-15 (new claims 16-29) have been rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for various reasons enumerated (a) through (h) in the Office Action. Applicants have amended the claims to address the Examiner’s concerns with respect to (a) the definition of A (defined variable A¹ and Z¹), (b) the definition of

Y (defined variable Y¹), (c) the definition of R⁸, (e) the unmatched closed bracket in original claim 8 (new claim 23), and (f) the erroneous period in original claim 8 (new claim 23).

The Office Action further questions certain numeric representations in original claims 8 and 12 (new claims 23 and 26) (*see* (d) and (g)). As would be apparent to a person of ordinary skill in the art, the numeric representation after some of the species of new claims 23 and 26 indicate the exact salt form. For example, the fourth species in new claim 23 is defined as 6,11-dihydrospiro[5-imidazo[2,1-b][3]benzazepine-11,4'-piperidine]-3-methanol] (E)-2-butenedioate (2:1). This indicates that the salt consists of 2 moieties of 6,11-dihydrospiro[5-imidazo[2,1-b][3]benzazepine-11,4'-piperidine]-3-methanol] and 1 butenedioate moiety.

Finally, the Office Action states that the term “derivatizing” in original claims 14 and 15 (new claims 28 and 29) implies more than what is positively recited (*see*, (h)). Applicants respectfully submit that the term “derivatize” is readily understood by those of ordinary skill in the art and that in the context of the claims would mean to derivatize in such a way that the resulting compound still falls within the scope of the claimed invention. The specification provides numerous examples of suitable derivation methods (*see, e.g.*, Specification at pages 8-23).

Based on the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejections under 35 U.S.C. §112, second paragraph.

Rejection Under 35 U.S.C. § 103

Original claims 1, 2 and 4-8 (new claims 16, 17 and 19-23) have been rejected under 35 U.S.C. § 103(a) as being obvious in view of Janssens *et al.*, WO 97/24356 (“Janssens”). In particular, it is asserted in the Office Action that that Applicants’ defined compounds are encompassed by the generic structure disclosed in Janssens (Formula III-a-2-1, page 12), and

that one of ordinary skill in the art would have been motivated to select Applicants' compounds from this generic disclosure. Applicants respectfully traverse this rejection as the compounds defined in the present claims are neither disclosed nor suggested by Janssens.

The present compounds are 4-(imidazo-azepine) piperidine spiro compounds that have been found to possess antihistaminic activity. In contrast, Janssens discloses 4-(imidazo-azepine) piperidine spiro derivatives as *intermediates* in the preparation of 1-(1,2-disubstituted piperidinyl)-4-(imidazo-azepine) piperidine spiro derivatives having tachykinin antagonistic activity.

In view of the Janssens teachings, it is respectfully submitted that one of ordinary skill in the art would have had no motivation to arrive at Applicants' claimed compounds. Obviousness may be established only if both the suggestion and reasonable expectation of success are founded in the prior art, not in Applicant's disclosure. *In re Vaeck*, 20 U.S.P.Q.2d 1438, 1442 (Fed. Cir. 1991). The mere possibility for modification of the prior art is not the motivating force that the law requires. If it were, then no modification would ever lack motivation since some change is always possible. Quite to the contrary, an invention is obvious under the patent laws only when the claimed means for effecting an improvement -- as opposed to the possibility of trying any and all means -- is suggested by the prior art. *In re Shaffer*, 108 U.S.P.Q. 326 (C.C.P.A. 1956).

In this case, Applicants respectfully submit that a person of ordinary skill in the art would have absolutely no motivation to look to Janssens in attempting to arrive at an antihistaminic compound, *i.e.*, the subject of Applicants' claims. Even if one of ordinary skill were to come across generic Formula III-a-2-1 disclosed in Janssens, it is respectfully submitted that there would be no motivation to select from this generic disclosure the antihistaminic

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compounds claimed by Applicants given that Formula III-a-2-1 represents an intermediate used in the synthesis of tachykinin antagonists. Applicants submit respectfully that the only motivation to do so comes from Applicants' disclosure itself.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 103 in view of Janssens.

Miscellaneous

Applicants have replaced original claim 11 with new claim 25 and removed the multiple dependency.

Applicants appreciate the Examiner's suggestion concerning providing reference in the Specification regarding related applications and have amended the specification accordingly. Applicants have also submitted an Abstract of the disclosure on a separate page (page 60), and request that the Abstract be entered.

Conclusion

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "Version with markings to show changes made." Entrance of the foregoing amendments and an early and favorable Action is respectfully requested.

Date: 1/27/03

Respectfully submitted,



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VERSION WITH MARKINGS TO SHOW CHANGES MADE**In the Specification**

Please insert the following paragraph after the title of the invention:

-- Cross Reference To Related Applications

This application is a national stage entry under 35 U.S.C. § 371 of PCT/EP99/10176, filed December 15, 1999. --

Please replace the paragraph beginning at page 2, line 20, with the following rewritten paragraph:

L represents a radical of formula

-Alk-Y¹-Het¹ (c-1),

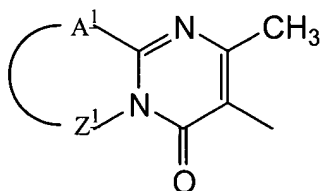
-Alk-NH-CO-Het² (c-2) or

-Alk-Het³ (c-3); wherein

Alk represents C₁₋₄alkanediyl;

Y¹ represents O, S or NH;

Please replace the paragraph (formula) beginning at page 3, line 1, with the following rewritten paragraph:



wherein

A¹-Z¹ represents S-CH=CH, S-CH₂-CH₂, S-CH₂-CH₂-CH₂, CH=CH-CH=CH, or CH₂-CH₂-CH₂-CH₂;

In the Claims

Claims 1-8 and 10-15 have been canceled. New claims 16-30 have been added.